Elevations of Serum T_3 Levels and Their Association With Symptoms in World War II Veterans With Combat-Related Posttraumatic Stress Disorder: Replication of Findings in Vietnam Combat Veterans

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Objective: In previous serum thyroid studies, we reported an unusual thyroid profile, including elevated levels of total and free triiodothyronine (T_3), total thyroxine (T_4), and thyroxine-binding globulin (TBG) with no elevations in free T_4 and thyrotropin (TSH) in Vietnam veterans with combat-related posttraumatic stress disorder (PTSD) compared to control subjects. In a subsample of Vietnam veterans, we found a significant positive correlation between total T_3, free T_3, and PTSD symptoms, specifically hyperarousal symptoms. In the present study, we explored the generalizability of our findings to World War II (WWII) veterans with PTSD. **Method:** Clinical symptoms were assessed in and serum thyroid measures were obtained from 12 WWII veterans with PTSD and 18 WWII veterans without PTSD. **Results:** WWII veterans with combat-related PTSD showed elevations of serum total and free T_3 with no elevations of free T_4 and TSH compared to control subjects, replicating the results of our previous studies. A significant positive relationship between total and free T_3 and PTSD symptoms, specifically hyperarousal symptoms, was also replicated in the total WWII group. Elevations of total T_4 and TBG were not replicated in the WWII group with PTSD, which may indicate a shift with age in the free/bound dynamics of the thyroid alterations observed. **Conclusions:** This study supports the observation that the thyroid system is altered in chronic combat-related PTSD. The observed alterations of thyroid function along with PTSD symptoms appear to be chronic, detectable 50 years after the war. **Key words:** posttraumatic stress disorder, thyroid, triiodothyronine, combat, World War II veterans, psychiatric symptoms.

PTSD = posttraumatic stress disorder; T_3 = triiodothyronine; T_4 = thyroxine; TSH = thyrotropin; WWII = World War II; TBG = thyroxine-binding globulin; PSS = PTSD Symptom Scale; POW = prisoner of war.

INTRODUCTION

Biological studies of traumatic stress in humans have focused mainly on the responses of the sympathetic-adrenal-medullary axis and the hypothalamic-pituitary-adrenal axis. Less attention has been given to the hypothalamic-pituitary-thyroid axis, although evidence of an important relationship between traumatic stress and thyroid function has a long history (1). In 1825, the original clinical report of hyperthyroidism by Parry (2) described the onset of symptoms in a woman 4 months after a terrifying experience in which she was accidentally thrown down the stairs in a wheelchair. This relationship between traumatic stress and thyroid function was extensively confirmed, as reviewed by Bram (3), who reported that a clear history of traumatic stress was found in 85% of more than 3000 cases of thyrotoxicosis. The precipitating conditions largely involved severe life-threatening crises, now commonly referred to as traumatic stress, such as fires, shipwrecks, earthquakes, combat experiences, and narrow escapes from accidents, as well as various types of object loss. The most striking common feature associated with these stressful experiences seems to be extreme fear concerning biological survival. More recent research continues to support the observation that patients with hyperthyroidism report a history of more stressful life events than do members of a control population (4–6). Animals studies also confirm alterations in thyroid hormone secretion in response to a variety of psychologically stressful situations (1).

With this rationale in mind, we added a complete thyroid assessment to our profile of stress-responsive hormonal measures in studying the psychoendocrinology of PTSD in combat veterans. In previous studies, we observed an unusual thyroid profile in these veterans, including elevated total T_3, free T_3, and total T_4, but no elevation of free T_4 or TSH compared to control subjects. We have replicated these findings in four groups (N = 96) of Vietnam combat veterans (7) and a group (N = 11) of Israeli combat veterans (8) with PTSD. The thyroid elevations did not typically exceed the normal range, as specified for the diagnosis of glandular disease in the field of clinical endocrinology, but there is evidence that relatively modest changes in thyroid hormone levels may have important clinical significance in relation to psychiatric disorders (9).

In exploring the clinical significance of the T_3 elevations in combat-related PTSD, we found significant

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positive correlations between total T_3, free T_3, and PTSD symptoms, specifically frequency of hyperarousal symptoms measured by the Clinician-Administered PTSD Scale in a sample ($N = 65$) of Vietnam veterans (10) and novelty seeking subscale scores on the Cloninger Tridimensional Personality Questionnaire in another sample ($N = 27$) of Vietnam veterans (11). Many of the symptoms of hyperthyroidism are similar to the hyperarousal symptoms observed in PTSD, for example, irritability, difficulty sleeping, difficulty concentrating, anger outbursts, and exaggerated startle. Because T_3 is two to four times more biologically active than T_4, the significant positive correlation between T_3 and hyperarousal seemed to provide evidence of a potentially important hormone-symptom relationship in this disorder. To determine whether these findings could be replicated and generalized more broadly in combat-related PTSD, we studied WWII veterans to investigate whether their biological characteristics, 50 years after the war, reflected the thyroid alterations and the hormone-symptom relationships we observed in younger Vietnam veterans.

METHODS

Subjects

WWII veterans with PTSD were recruited from outpatient WWII PTSD groups at VA Connecticut on the West Haven and Newington campuses. Veterans without PTSD were recruited from "Later Life Issues" outpatient groups at the same locations. Additional veterans, recruited for a comparison group from the clinical laboratory at the West Haven campus, were having blood drawn for routine physicals or other reasons and agreed to participate in the research study by having an extra tube of blood drawn. Not all the subjects in the PTSD group met the criteria for PTSD in this study (Mississippi Scale score > 107), and their data ($N = 3$) were analyzed as part of the comparison group. Conversely, some of the subjects recruited for the comparison group did meet criteria for PTSD, and their data ($N = 3$) were analyzed as part of the PTSD group. Exclusion criteria included psychotic disorders, current use of thyroid hormone medication, organic brain syndrome, and current drug or alcohol abuse.

Hormonal Samples

Blood samples (10 ml) in red-topped (untreated) vacuum tubes for thyroid hormone assays were collected between 8 and 9 AM in 27 of the 30 subjects; three blood samples were collected later in the day. After setting of the clot and centrifugation, the serum was divided into three 1.5-ml aliquots in small glass vials and frozen at −70°C until assayed. Because six different hormonal assays were to be performed on each sample, the three aliquots minimized freezing and rethawing cycles as a potential source of hormonal instability and analytic error, especially since two different hormonal assays were usually done concurrently when each aliquot was thawed.

Serum total T_4, free T_4, total T_3, and TBG concentrations were measured by radioimmunoassay (RIA) procedures using commercially available kits (Incstar Corp., Stillwater, MN). The interassay coefficient of variation in our laboratory was 3.7% for total T_4, 4.2% for free T_4, 6% for total T_3, and 4.0% for TBG. Serum-free T_3 concentrations were measured using an RIA kit procedure (Diagnostic Products Corp., Los Angeles, CA). The interassay coefficient of variation in our laboratory was 2.7% for free T_3. Serum TSH concentrations were measured by means of a sensitive third-generation immunoradiometric procedure (Incstar Corp.), and the interassay coefficient of variation was 4.0% in our laboratory.

Clinical Measures

The following clinical measures were administered to assess PTSD symptoms, combat exposure, and general psychiatric symptomatology: the Mississippi Scale for Combat-Related PTSD (12); the PTSD Symptom Scale (PSS) (13), which includes symptom cluster subscales; the Combat Exposure Scale (14); and the Brief Symptom Inventory (15). As stated above, the criterion for a diagnosis of PTSD was a Mississippi Scale score of 107 or above. Age, height, weight, years of education, medical problems, medications, and history of or current substance abuse, smoking, and suicidality were obtained during an interview with each subject. When possible, information was confirmed by hospital records.

Data Analysis

All thyroid measures were included in an overall one-factor multivariate analysis of variance to determine whether there were overall mean differences between the two groups when all dependent variables were considered simultaneously. Subsequent univariate t tests were performed on each dependent variable. Pearson product-moment correlations were used for correlational analyses. On the basis of our previous work, we predicted higher thyroid hormone levels in the PTSD group and positive correlations between thyroid measures and clinical measures. Therefore, we used one-tailed probability values for all t tests and individual correlation coefficients. Bonferroni probability values were calculated to correct for the number of correlations in the correlation matrix.

RESULTS

Thyroid Measures

A multivariate analysis of variance including all thyroid measures showed a significant overall mean difference between the PTSD and comparison groups. Mean values ± standard errors of the means for subsequent individual t tests are summarized in Table 1. Significant elevations of serum total T_3, free T_3, and the total T_3/free T_4 ratio were found in the WWII PTSD group compared to control subjects. No significant mean differences were found in levels of total T_4, free T_4, TBG, or TSH between the two groups.

Individual correlation coefficients and significant probability values ($\alpha < .05$) for correlations between thyroid measures and clinical measures of PTSD are shown in Table 2. Correlations that are also significant after correction for the number of correlations in the matrix using the Bonferroni procedure are indicated. The strength of the positive correlation between both total and free T_3 and hyperarousal symptoms, measured by the PSS, is supported by a finding of significance after correction for multiple correlations.

TABLE 1. Mean (±SEM) Serum Thyroid Measures in WWII Veterans With and Without PTSD

Group	Total T_3 (ng/dl)	Free T_3 (pg/ml)	Total T_4 (μg/dl)	Free T_4 (ng/dl)	TBG (μg/ml)	TSH (μIU)	TT_3:FT_3 Ratio
With PTSD,	177[a]	3.45[a]	8.3	1.31	31.7	2.21	138[b]
N = 12	(±8.69)	(±0.11)	(±0.34)	(±0.06)	(±1.89)	(±0.41)	(±9.4)
Without PTSD,	152	3.01	8.4	1.35	28.7	1.46	115
N = 18	(±3.93)	(±0.08)	(±0.38)	(±0.05)	(±1.74)	(±0.29)	(±5.3)

[a] $p < .01$.
[b] $p < .05$.

TABLE 2. Correlations Between Thyroid Measures and Clinical Measures (N = 30)

Measure	Serum T_3		Serum T_4		TBG	TSH
	Total	Free	Total	Free		
Mississippi Scale	$r = .41$	$r = .61$[a]	$r = .05$	$r = -.11$	$r = .31$	$r = .32$
	$p < .01$	$p < .0002$	$p < .38$	$p < .30$	$p < .05$	$p < .04$
PSS						
Reexperiencing	$r = .36$	$r = .48$	$r = .06$	$r = -.01$	$r = .23$	$r = .17$
	$p < .03$	$p < .004$	$p < .37$	$p < .47$	$p < .11$	$p < .19$
Avoidance	$r = .30$	$r = .55$[b]	$r = .01$	$r = -.07$	$r = .20$	$r = .10$
	$p < .06$	$p < .0008$	$p < .50$	$p < .36$	$p < .14$	$p < .30$
Hyperarousal	$r = .53$[b]	$r = .60$[a]	$r = .05$	$r = -.10$	$r = .35$	$r = .23$
	$p < .001$	$p < .0003$	$p < .39$	$p < .30$	$p < .03$	$p < .10$
Total	$r = .40$	$r = .56$[b]	$r = .03$	$r = -.06$	$r = .25$	$r = .17$
	$p < .02$	$p < .0006$	$p < .44$	$p < .37$	$p < .09$	$p < .18$
Combat Exposure Scale	$r = .33$	$r = .31$	$r = .24$	$r = .29$	$r = .14$	$r = -.10$
	$p < .05$	$p < .06$	$p < .11$	$p < .07$	$p < .29$	$p < .31$

[a] $p < .01$ after Bonferroni correction for number of correlations.
[b] $p < .05$ after Bonferroni corrections for number of correlations.

Serum Total T_3

As shown in Table 1, WWII veterans with PTSD had significantly higher mean levels of serum total T_3 than WWII veterans without PTSD (177 vs. 152 ng/dl, $t = 2.71$, $p < .008$). A significant positive correlation (Table 2) was found between serum total T_3 and the hyperarousal subscale of the PSS ($r = .53$, $p < .001$). This correlation was also significant at the .05 level after Bonferroni correction for multiplicity. Significant positive individual correlations (Table 2) were found between total T_3 and the total Mississippi Scale score, the PSS reexperiencing subscale, the PSS total score, and the Combat Exposure Scale score, but none of these correlations reached significance after Bonferroni correction.

Serum-Free T_3

Table 1 shows significantly higher mean levels of serum-free T_3 in WWII veterans with PTSD compared to WWII veterans without PTSD (3.45 vs. 3.01 pg/ml, $t = 3.38$, $p < .001$). Significant positive individual correlations were found between serum-free T_3 and each clinical PTSD measure administered: the Mississippi Scale score, the PSS total score, and each PSS subscale (reexperiencing, avoidance, and hyperarousal). After Bonferroni corrections were made, only the reexperiencing subscale of the PSS failed to reach significance at the .05 level. Highly significant positive correlations were observed between serum-free T_3 and both the hyperarousal subscale of the PSS (Figure 1; $r = .60$, $p < .0003$) and total Mississippi Scale scores ($r = .61$, $p < .0002$). Both correlations were significant at the .01 level after Bonferroni correction for multiplicity. The individual correlation between serum-freeT_3 and the Combat Exposure Scale score was comparatively weak and of borderline positive significance ($r =.31$, $p < .06$).

Serum Total and Free T_4

There were no significant mean differences in total T_4 (8.3 vs. 8.4 μg/dl, $t = .22$, $p < .42$) or free T_4 (1.31 vs. 1.35 ng/dl, $t = .52$, $p < .31$) between the two groups. No significant correlations were found be-

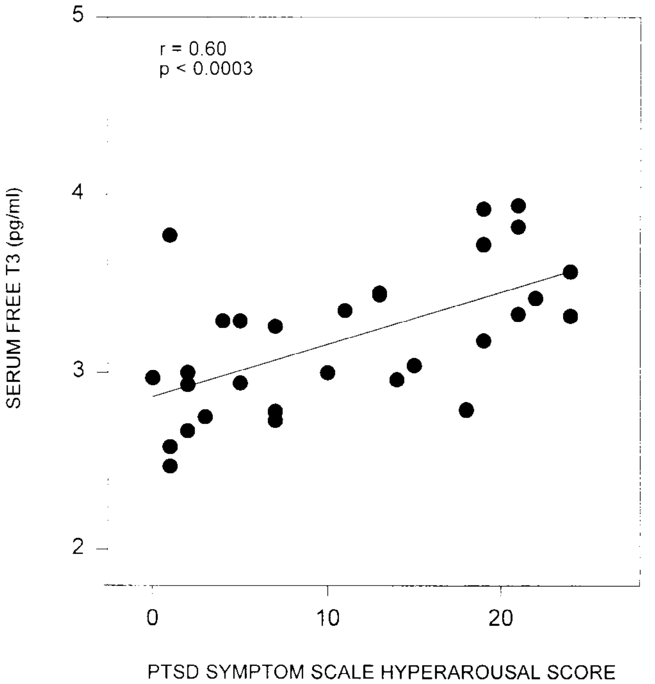

Fig. 1. Relationship between serum-free T_3 and PSS hyperarousal scores in WWII veterans ($N = 30$).

tween total and free T_4 and any clinical measures of PTSD used in the study.

Total T_3/Free T_4 Ratio

Previously, we hypothesized (6) that because about 80% of the body's supply of T_3 is produced by peripheral conversion of free T_4 to T_3, elevations of free and total T_3 found in combat-related PTSD patients might reflect increased peripheral conversion and that a useful indicator of the rate of the conversion process might be the total T_3/free T_4 ratio. A higher ratio would accordingly represent increased conversion of free T_4 to T_3. A significantly higher total T_3/free T_4 ratio (138 vs. 115, $t = 2.32$, $p < .014$) was found in WWII veterans with PTSD compared to WWII veterans without PTSD, supporting the hypothesis of increased conversion of free T_4 to T_3.

Serum TBG

No significant mean difference in serum TBG was found between the PTSD group and the comparison group (31.7 vs. 28.7 μg/ml, $t = 1.16$, $p < .13$). Both groups had relatively high levels of TBG (reference range: 12–30 μg/ml). Significant individual correlations between TBG and the Mississippi Scale score and the PSS hyperarousal subscale were found (Table 2; $r = .31$, $p < .05$ and $r = .35$, $p < .03$, respectively); however, after Bonferroni correction, no significant correlations were observed between TBG and any clinical measures of PTSD.

Serum TSH

No significant mean difference in serum TSH between the two groups was observed, although there was a trend toward higher TSH in the PTSD group (2.21 vs. 1.46 μIU, $t = 1.53$, $p < .07$). This could indicate the contribution of increased central drive to the elevations of T_3 in addition to the hypothesized augmented peripheral conversion of T_4 to T_3 in this population. In our previous studies with Vietnam and Israeli veterans, we did not observe a trend toward higher TSH. The individual correlation between the Mississippi Scale score and TSH was significant ($r = .32$, $p < .04$); however, it failed to reach significance after Bonferroni correction.

Clinical Measures

WWII veterans with PTSD reported significantly more symptoms on every clinical measure administered and almost twice the amount of combat exposure as WWII veterans without PTSD. The level of combat in the comparison group was light to moderate and in the PTSD group was moderate to heavy. Because the criteria for dividing the two groups was based on a score of 107 or more on the Mississippi Scale, it was expected that the other PTSD measures would also be quite different in the two groups. Scores from the Brief Symptom Inventory, which was designed to reflect general psychological symptom status, were also significantly elevated in the PTSD group (mean General Severity Index, 2.5 vs. 1.0, $t = 5.6$, $p < .001$). The subscales of the Brief Symptom Inventory include somatization, obsessive-compulsive behavior, interpersonal sensitivity, depression, anxiety, hostility, phobic anxiety, paranoid ideation, psychoticism, and additional items. This finding indicates that chronic PTSD does not simply result in elevated core symptoms associated with PTSD but seems to be related to a broad range of psychological symptoms.

Suicidality

History of suicidal thoughts was reported significantly more frequently in the PTSD group than in the comparison group (67% vs. 22%, $\chi^2 = 5.93$, $p = .015$).

Age, Height, Weight, Years of Education, Medical Problems, Substance Abuse, and Smoking

There were no significant mean differences in age (71.4 vs. 72 years), height (68 vs. 69 inches), weight (187 vs. 191 lb), or years of education (12.2 vs. 12.1 years) between the PTSD and comparison groups. Chi-square analyses of frequency of medical problems based on several categories (asthma, hypertension, diabetes, cardiovascular incident, heart disease, ulcer, cancer, emphysema, gastrointestinal problems, and miscellaneous medical problems) showed no significant differences in frequency of these medical conditions between the two groups. No differences (frequency) in history of or current substance abuse or smoking were found between the PTSD and comparison groups.

Medications

Most of the subjects in both groups were taking various medications. For statistical comparison, medications were grouped into three categories: psychiatric, cardiovascular, and other medications. Chi-square analyses showed no significant differences in frequency of prescription medications between the two groups in any category.

DISCUSSION

Hormonal Measures

The current findings of elevated total and free T_3 with no elevation of free T_4 and TSH in WWII combat veterans with PTSD replicate our previous findings in Vietnam (7) and Israeli combat veterans (8). To detect a significant elevation in T_3 in this elderly population, many of whom have significant medical problems, is quite striking because T_3 tends to decrease with age and chronic illness (16).

The normal range for serum total T_3 is 70 to 190 ng/dl (17). In our previous thyroid study (7), the control group (mean age = 38 years, $N = 24$) value for total T_3 was 127 ± 24 ng/dl. Considering the observation that T_3 tends to decrease with age, the WWII veterans in both the PTSD and comparison groups in the present study had marked elevations (177 and 152 ng/dl, respectively). Given the level of combat and perhaps partial PTSD in our comparison group, an age-matched civilian control group might reveal an even more dramatic elevation of T_3 in WWII veterans with PTSD.

Elevations of total T_4 and TBG previously observed in younger combat veterans with PTSD (6) were not observed in the older WWII PTSD group. This difference might be explained by the increased production of TBG observed in the elderly (18–19). Because TBG levels were elevated in both elderly groups and because TBG has a higher affinity for T_4, it follows that the differences in total T_4 between the PTSD and comparison groups would be reduced. To a lesser extent, because TBG has a lower affinity for T_3, the same dynamic holds true for total T_3. Therefore, the increased TBG production due to aging might have concealed some of the differences in bound thyroid hormones between the two elderly groups. Our findings of more significant elevations of *free* T_3 in older combat veterans with PTSD and more significant elevations of *total* T_3 in younger Vietnam combat veterans with PTSD support this notion. A similar pattern emerges in the T_3-symptom correlations, with *free* T_3 being most significantly related to symptoms in the older group and *total* T_3 being most significantly related to symptoms in younger combat veterans.

The total T_3/free T_4 ratio was significantly elevated in the WWII PTSD group, replicating our earlier finding in Vietnam veterans with PTSD and providing additional support for the hypothesis of increased peripheral conversion of T_4 to T_3 in combat-related PTSD (7). In contrast to the Vietnam veterans with PTSD, the WWII PTSD group had a nonsignificant trend toward higher TSH compared with control subjects, which may suggest that central nervous system drive, in addition to peripheral conversion, may contribute to the elevated T_3 measures observed in the older veterans.

The consistent and robust elevations in T_3 we have observed in veterans with combat-related PTSD were probably not detected in routine clinical thyroid function tests because, in general, they do not include direct measures of T_3. Although elevations of T_3 in this group are largely still within the normal range as defined in the field of clinical endocrinology and do not indicate glandular pathology, the strong positive correlations between T_3 and PTSD symptoms, specifically hyperarousal symptoms, seem to point to a potentially clinically significant hormone-symptom relationship. Replication of this relationship in two different groups of combat veterans with PTSD a full generation apart may indicate a need for further study of the clinical importance of T_3 levels in this population.

The question of whether symptoms occur in response to higher levels of T_3 or whether higher levels of T_3 occur in response to increased symptoms indicates a need for placebo-controlled pharmacologic studies whereby T_3 is lowered and clinical symptoms are monitored. The few open trials using propranolol, which lowers T_3, to treat PTSD symptoms have reported positive results (20–21). Because the complete role of T_3 in relation to PTSD symptoms is not yet clear, pilot studies in which there is careful monitoring of clinical responses to lowering T_3 should be completed before a large trial is initiated, because although T_3 seems to be related to disturbing PTSD symptoms, elevations of T_3 could have an adaptive purpose, perhaps modifying other types of symptoms or physiologic processes.

Clinical Measures

The chronicity of PTSD symptoms as well as other psychological symptoms in WWII veterans due to combat stress has been documented extensively in the literature by investigators at many specific time points [eg, 5 (22), 9 (23), 20 (24), 24 (25), and 50 years after the war (26)] and by several investigators (27–29). Our clinical data support the findings of previous studies of the chronicity of PTSD symptoms in WWII veterans and point to a general increase in overall psychological symptoms in this group.

It has been suggested that the neurobiological changes observed in PTSD may have more to do with exposure to traumatic stress than with PTSD. Although our sample size ($N = 30$) is somewhat small for correlational analyses, our finding that the probability value for the correlation between free T_3 and PTSD symptoms ($p < .0002$) is 200 times more significant than the probability value for the correlation between free T_3 and reported combat exposure ($p < .06$) seems to indicate that the thyroid alterations observed in these veterans may be more specifically related to the disorder of PTSD than to combat exposure alone.

Specificity of Thyroid Findings in PTSD

The consistency and robustness of the T_3 elevations observed in veterans with combat-related PTSD in different regional populations, cultures, and age groups strongly suggests that the thyroid system is significantly altered in this population.

We have observed a specific relationship between combat-related PTSD and elevations in serum total and free T_3. PTSD as a result of other traumatic experiences may reveal different thyroid profiles. Our preliminary work with POWs with PTSD suggests that these men do not have elevations in total and free T_3. A pilot sample population of five WWII POWs and three Korean War POWs had total and free T_3 levels significantly *below* the control group mean. The POWs' descriptions of their traumatic experiences and their adaptive responses to those experiences makes apparent that they speak in very different terms compared to combat veterans who were not POWs. For example, combat veterans often talk about intensive fighting or fleeing in response to combat. In contrast, POWs report that a fighting or fleeing strategy would likely get them killed. Instead, they describe a withdrawal strategy in terms of "shutting down" or "stonewalling" as an adaptive response to the traumatic stress of long-term captivity. Similarly, decreased levels of thyroid hormones were reported in a recent study of East German refugees suffering from psychiatric disorders, including PTSD, after exposure to prolonged stress (30). These refugees were subjected to unpredictable acts of repression and persecution by the State Security Police, including frequent summonses, interrogations, imprisonment, surveillance at home and work, and other forms of harassment.

Differences in adaptive responses to traumatic stress, partly determined by environmental constraints, may influence whether the thyroid system is activated or suppressed. It is possible that physiologic responses to a chronic life-threatening situation can elevate thyroid hormones, stimulate the sympathetic-adrenal-medullary fight-or-flight system, and result in resetting of the metabolic system toward mobilization and catabolism. However, if the traumatic events occur in an environment in which the fight-or-flight response is not adaptive for survival (eg, in a POW situation, the Holocaust, an oppressive political situation, or some domestic abuse situations), then a life-threatening stressor could result in an adaptation toward conservation/withdrawal and a resetting of the metabolic system toward conservation, anabolism, and decreased thyroid measures. Henry (31) has discussed the contrast in neuroendocrine profiles as the result of active vs. passive coping strategies in response to perceived threat. More specific attention to the adaptive mechanisms used to survive the trauma may be warranted to more fully understand the role of thyroid hormones in PTSD. This point is important to consider because our data do not suggest that all patients meeting criteria for PTSD will have elevated T_3 levels. Additional thyroid studies in different PTSD populations with attention given to both short- and long-term adaptive strategies used in response to traumatic experiences will help to clarify the specificity of thyroid alterations in PTSD.

Limitations

The number of subjects ($N = 30$) in this study was small for correlational analyses. Perhaps a larger sample might reveal significant associations between thyroid hormones and other measures (eg, the Combat Exposure Scale). Correlational analyses do not imply causality. From our study, there is no way to determine whether combat veterans with PTSD had elevations in T_3 before they were exposed to combat trauma and were more vulnerable to developing PTSD symptoms or whether T_3 elevations occurred after their combat exposure and consequently were associated with symptoms.

CONCLUSION

The significantly higher mean levels of total T_3, free T_3, and the total T_3/free T_4 ratio observed in WWII combat veterans with PTSD compared with WWII veterans without PTSD support our previous observation that the thyroid system is altered in combat-related PTSD. The present T_3 results replicate our previous findings in Vietnam and Israeli veterans in another population whose members were of a totally different age group and participated in a different war at a different time in history. The consistent finding of elevated T_3 in PTSD combat veterans across cultures and across age groups strongly suggests the generalization of T_3 as a biological marker for combat-related PTSD.

The current replication of a significant positive relationship between T_3 and PTSD symptoms, especially hyperarousal symptoms, provides additional evidence of a potentially important T_3-hyperarousal symptom association and may offer a rationale for assessment of T_3 and pharmacologic intervention to reduce T_3 in combat-related PTSD.

Preliminary data indicate that T_3 is not elevated and may be decreased in WWII and Korean War POWs, suggesting that elevations of T_3 may be specific to combat-related PTSD. Other PTSD populations exhibiting different adaptations to traumatic experiences, perhaps due to environmental constraints, may also show distinct thyroid profiles.

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